A Study to Test the Addition of the Drug Cabozantinib to Chemotherapy in Patients With Newly Diagnosed Osteosarcoma

Status: RECRUITING

Eligibility Criteria

Age: Up to 40 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* Patients must be \< 40 years of age at the time of enrollment. * Patients must have a body surface area of \>= 0.8 m\^2 at the time of enrollment. * Patients must have histologic diagnosis (by institutional pathologist) of newly diagnosed high grade osteosarcoma. Primary tumors of all extremity and axial sites are eligible as long as diagnosis of high-grade osteosarcoma is established. Osteosarcoma as a second malignancy is eligible if no prior exposure to systemic chemotherapies. * Feasibility Phase (NOTE: as of Amendment #2B, the feasibility phase has been completed) Patients must have metastatic disease and a resectable primary tumor. Designation of a primary tumor as resectable will be determined at the time of diagnosis by the institutional multidisciplinary team. For this study, metastatic disease is defined as one or more of the following: * Lesions which are discontinuous from the primary tumor, are not regional lymph nodes, and do not share a bone or body cavity with the primary tumor. Skip lesions in the same bone as the primary tumor do not constitute metastatic disease. Skip lesions in an adjacent bone are considered bone metastases. * Lung metastases: defined as biopsy-proven metastasis or the presence of one or more pulmonary lesions \>= 5 mm, OR multiple pulmonary lesions \>= 3 mm or greater in size. * Bone metastases: Areas suspicious for bone metastasis based on fludeoxyglucose F-18 (18F-FDG)-positron emission tomography (PET) scan (or whole body technetium-99 bone scan if 18F-FDG-PET is unavailable at the treating institution) require confirmatory biopsy or supportive anatomic imaging of at least one suspicious site with either magnetic resonance imaging (MRI) or computed tomography (CT) (whole body 18F-FDG-PET/CT or 18F-FDG-PET/MR scans are acceptable). * Efficacy Phases (Phase 2/3) NOTE: as of Amendment #2B, the efficacy phase is open for enrollment. Patients with both localized and metastatic disease are eligible for the efficacy phase, regardless of resectability. Patients will be enrolled to two separate cohorts: * Cohort 1 (Standard Risk): Patients with non-pelvic primary osteosarcoma deemed to be resectable at the time of diagnosis by the institutional multidisciplinary team, without evidence of metastatic lesions. * Cohort 2 (High-Risk): Patients with a primary pelvic tumor, a primary tumor designated as unresectable by the institutional multidisciplinary team, AND/OR radiographic evidence of metastatic lesions. * A serum creatinine based on age/sex as follows (within 7 days prior to enrollment unless otherwise indicated): * (Age: Maximum Serum Creatinine \[mg/dL\]; Sex) * 1 month to \< 6 months: 0.4 (male); 0.4 (female) * 6 months to \< 1 year: 0.5 (male); 0.5 (female) * 1 to \< 2 years: 0.6 (male); 0.6 (female) * 2 to \< 6 years: 0.8 (male); 0.8 (female) * 6 to \< 10 years: 1 (male); 1 (female) * 10 to \< 13 years: 1.2 (male); 1.2 (female) * 13 to \< 16 years: 1.5 (male); 1.4 (female) * \>= 16 years: 1.7 (male); 1.4 (female) * OR

•a 24 hour urine creatinine clearance \>= 70 mL/min/1.73 m\^2 * OR

•a glomerular filtration rate (GFR) \>= 70 mL/min/1.73 m\^2. GFR must be performed using direct measurement with a nuclear blood sampling method OR direct small molecule clearance method (iothalamate or other molecule per institutional standard). * Note: Estimated GFR (eGFR) from serum creatinine, cystatin C or other estimates are not acceptable for determining eligibility. * Total bilirubin =\< 1.5 x upper limit of normal (ULN) for age (within 7 days prior to enrollment unless otherwise indicated) * Serum glutamate pyruvate transaminase (SGPT) (alanine aminotransferase \[ALT\]) =\< 135 U/L (within 7 days prior to enrollment unless otherwise indicated) * Note: For the purpose of this study, the ULN for SGPT (ALT) has been set to the value of 45 U/L * No history of congenital prolonged corrected QT (QTc) syndrome, New York Heart Association (NYHA) Class III or IV congestive heart failure, unstable angina pectoris, serious cardiac arrhythmias * Shortening fraction of \>= 27%, or * Ejection fraction of \>= 50% * Corrected QT interval by Fridericia (QTcF) \< 480 msec on electrocardiogram. Patients with Grade 1 prolonged QTc (450-480 msec) at time of study enrollment should have correctable causes of prolonged QTc addressed if possible (i.e., electrolytes, medications). * Peripheral absolute neutrophil count (ANC) \>= 1000/uL (within 7 days prior to enrollment unless otherwise indicated) * Platelet count \>= 100,000/uL (transfusion independent, defined as not receiving platelet transfusions within a 7-day period prior to enrollment) (within 7 days prior to enrollment unless otherwise indicated) * Hemoglobin \>= 8.0 g/dL (within 7 days prior to enrollment unless otherwise indicated) * International normalized ratio (INR) =\< 1.5 (within 7 days prior to enrollment unless otherwise indicated) * Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible as long as they are NOT receiving anti-retroviral agents that are strong inhibitors or inducers of CYP3A4, CYP2D6, and/or MRP2 transporter protein. * All patients and/or their parents or legal guardians must sign a written informed consent. * All institutional, Food and Drug Administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met.

Exclusion Criteria:

* Patients who have received previous systemic therapy for osteosarcoma or a prior oncologic diagnosis. * Patients who have central nervous system metastases. * Patients with central cavitating pulmonary lesions invading or encasing any major blood vessels in the lung. * Patients who are unable to swallow tablets. Tablets cannot be crushed or chewed. * Patients with gastrointestinal disorders including active disorders associated with a high risk of perforation or fistula formation. Specifically, no clinically significant gastrointestinal (GI) bleeding, GI perforation, bowel obstruction, intra-abdominal abscess or fistula for 6 months prior to enrollment, no hemoptysis or other signs of pulmonary hemorrhage for 3 months prior to enrollment. * Patients with active bleeding or bleeding diathesis. No clinically significant hematuria, hematemesis, or hemoptysis or other history of significant bleeding within 3 months prior to enrollment. * Patients with uncompensated or symptomatic hypothyroidism. Patients who have hypothyroidism controlled with thyroid replacement hormone are eligible. * Patients with moderate to severe hepatic impairment (Child-Pugh B or C). * Patients who have had primary tumor resection or attempted curative resection of metastases prior to enrollment. * Patients who have undergone other major surgical procedure (eg, laparotomy) within 14 days prior to enrollment. Thoracoscopic procedures for diagnostic purposes (biopsy of lung nodule) and central access such as port-a-cath placement are allowed. * Patients with a history of serious or non-healing wound or bone fracture (pathologic fracture of primary tumor is not considered exclusion). * Patients with any medical or surgical conditions that would interfere with gastrointestinal absorption of cabozantinib. * Patients with previously identify allergy or hypersensitivity to components of the study treatment formulations. * Patients who are receiving any other investigational agent not defined within this protocol are not eligible. * Patients who in the opinion of the investigator may not be able to comply with the safety monitoring requirements of the study are not eligible. * Patients who received enzyme-inducing anticonvulsants within 14 days prior to enrollment. * Patients with a prior history of hypertension (\> 95th percentile for age, height, and sex for patients \< 18 years and \> 140/90 mmHg for patients \>= 18 years requiring medication for blood pressure control. * Patients who are receiving drugs that prolong QTc. * Patients receiving anticoagulation with oral coumarin agents (eg warfarin), direct thrombin inhibitors (eg dabigatran), direct factor Xa inhibitor betrixaban, or platelet inhibitors (eg, clopidogrel). Low dose aspirin for cardioprotection (per local applicable guidelines) and low dose, low molecular weight heparins (LMWH) are permitted. Anticoagulation with therapeutic doses of LMWH and direct factor Xa inhibitors rivaroxaban or apixaban are allowed in subjects who are on a stable dose for at least 6 weeks before the first dose of study treatment, and who have had no complications from a thromboembolic event or the anticoagulation regimen. * Patients receiving strong CYP3A4 inducers or strong CYP3A4 inhibitors. * Female patients who are pregnant since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required for female patients of childbearing potential. * Lactating females who plan to breastfeed their infants. * Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of protocol therapy.

Conditions & Interventions

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Interventions:
PROCEDURE: Bone Scan, DRUG: Cabozantinib S-malate, DRUG: Cisplatin, PROCEDURE: Computed Tomography, DRUG: Doxorubicin Hydrochloride, PROCEDURE: Magnetic Resonance Imaging, DRUG: Methotrexate, PROCEDURE: Surgical Procedure, PROCEDURE: X-Ray Imaging
Conditions:
High Grade Osteosarcoma, Localized Osteosarcoma, Metastatic Osteosarcoma, Secondary Osteosarcoma

More Information

Contact(s): ctrrecruit@vcu.edu
Principal Investigator:
Phase: PHASE2
IRB
Number:
System ID: NCT05691478
